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Prevalence, predictors and prognostic significance of microalbuminuria in acute cardiac patients: a single center experience

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Abstract The objective of this study was to prospectively assess the prevalence, predictors and prognostic significance of microalbuminuria in a large cohort of consecutive acute cardiac patients, admitted to an intensive cardiac care unit from 1 January 2008 to 30 June 2009. In 815 acute cardiac patients, microalbuminuria is detectable in 39.3%. Microalbuminuria shows a significant negative correlation with left ventricular ejection fraction (Spearman's $\rho = -0.228$; $p < 0.001$), while it is positively correlated with C-reactive protein (Spearman's $\rho = 0.239$; $p < 0.001$), NT-pro-BNP (Spearman's $\rho = 0.306$; $p < 0.001$) and glycemia (Spearman's $\rho = 0.191$; $p < 0.001$). Microalbuminuria is an independent predictor for in-hospital mortality (1 $\mu\text{g}/\text{min}$ step) (OR 1.015; 95% CI 1.008–1.023; $p < 0.001$). In the acute phase of cardiac patients, microalbuminuria is a common finding, and it represents an independent predictor for early mortality. It is strictly linked to the inflammatory activation (as indicated by C-reactive protein) and to acute glucose values, thus suggesting that it may be part of the acute response to stress.

Keywords Microalbuminuria · Acute cardiac patients · Prognosis · C-reactive protein

Introduction

Microalbuminuria is a known marker of vascular permeability and endothelial dysfunction, and has been found to be predictive of outcome in a wide variety of chronic and acute conditions such as neoplastic disease [1, 2], surgery [3], acute pancreatitis [4] and trauma [5].

In acute setting, microalbuminuria has been shown to be a useful tool to predict illness severity and outcome in critically ill adult patients admitted to an intensive care unit (ICU) [6–8], but in these studies acute cardiac patients are scarcely or not represented. Gopal et al. [6] report that microalbuminuria predicts ICU mortality and inotrope requirement, as well as or better than APACHE II and SOFA scores in a mixed population (including about 10% cardiac surgery patients). Similar results are reported by Abid et al. [7] in a small subset of 40 medical patients (three patients with cardiorespiratory arrest), and by Thorevska et al. [9] in 104 critically ill patients (sepsis was present in the 43.3% of all population).

The aim of the present investigation was therefore to prospectively assess the prevalence, predictors and prognostic significance of microalbuminuria in a large cohort of consecutive acute cardiac patients, admitted to our intensive cardiac care unit (ICCU).

Methods

We prospectively enrolled all 888 patients admitted to our ICCU from 1 January 2008 to 30 June 2009. Exclusion

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criteria were as follows: pre-existing chronic renal failure (60 patients), no urine output on the first day of admission, on renal replacement therapy, or overtly bloody urine (13 patients) [9]. Our study population was 815 patients.

Microalbuminuria was measured on the first day of admission (in the overnight urine collection), and was defined as ranging from 20 to 200 µg/min [10]. On ICCU admission, after PCI, in a fasting blood sample the following parameters were measured: glucose (g/l), troponin I (Tn I, ng/ml), uric acid (mg/dl) [11], NT-pro brain natriuretic peptide (NT-BNP) (pg/ml) [12], leukocytes count ($\times 10^3/\mu\text{l}$), fibrinogen (mg/dl), erythrocyte sedimentation rate (ESR), lactate, C-reactive protein (C-RP, mg/dl). Creatinine (mg/dl) was also measured in order to calculate glomerular filtration rate ($\text{ml/min}/1.73 \text{ m}^2$) [13]. Glucose values were measured three times a day and peak glucose was considered. In patients with STEMI and UA/NSTEMI Tn I was measured three times a day and peak Tn I was reported [11, 12].

Transthoracic 2-dimensional echocardiography was performed on ICCU admission in order to measure left ventricular ejection fraction (LVEF).

In-ICCU mortality was the end point of outcome in our study.

Statistical analysis

Data were processed by means of SPSS 13.0 statistical package (SPSS Inc., Chicago, IL, USA). A two-tailed p value <0.05 was considered statistically significant. Data are reported as frequencies (percentages) and medians [95% Confidence Interval (CI)] and analyzed by means of

χ^2 (or Fisher's exact test, when appropriate) and Mann-Whitney U test. By means of Spearman's rho the correlations between the presence of microalbuminuria, LVEF, C-reactive protein, admission glycemia and NT-pro BNP were assessed. A backward stepwise logistic regression analysis was conducted in order to identify the variables correlated to microalbuminuria and in-ICCU death. In the logistic models, candidate variables were chosen as those that were significantly different at univariable analysis, or were clinically relevant. Backward procedure (probability for entry 0.05; probability for removal 0.10) was repeated until all variables in the model reached statistical significance. For each model, calibration was assessed by means of a Hosmer-Lemeshow goodness of fit test; pseudo R^2 were also assessed. Receiver operating characteristic (ROC) curves were constructed for microalbuminuria and in-ICCU death.

Results

Our series comprises the following subgroups according to admission diagnosis, as follows:

1. ST elevation myocardial infarction [14]: in our hospital, in Florence, the reperfusion strategy of STEMI patients is represented by primary PCI [12]. The patients are first evaluated by the Medical Emergency System in the pre-hospital setting, and then directly admitted to the catheterization laboratory or transferred to it after a rapid stabilization in the emergency department (ED). After primary PCI, they are admitted to our ICCU.

Table 1 Clinical Characteristics of the 815 patients included into the study

| | Median (IR) or frequency (%) |
|---------------------------------------|------------------------------|
| Age [median (IR), years] | 72 (62–79) |
| Gender [Males/Females, frequency (%)] | 549/266 (67.4/32.6) |
| <i>Comorbidities</i> | |
| Diabetes mellitus [frequency (%)] | 200 (24.5) |
| Hypertension [frequency (%)] | 524 (64.3) |
| <i>Diagnoses</i> | |
| STEMI [frequency (%)] | 252 (30.9) |
| UA/NSTEMI [frequency (%)] | 330 (40.5) |
| Acute heart failure [frequency (%)] | 81 (9.9) |
| Arrhythmias [frequency (%)] | 36 (4.4) |
| Other [frequency (%)] | 116 (14.2) |
| LOS [median (IR), h] | 72 (48–96) |
| In-ICCU mortality [frequency (%)] | 33 (4.0) |

IR interquartile range, STEMI ST elevation myocardial infarction, UA/NSTEMI unstable angina/Non ST elevation myocardial infarction, LOS length of stay, ICCU intensive cardiac care unit

Table 2 Comparison between patients with and without microalbuminuria

| | No microalbuminuria 469 (57.5%) | Microalbuminuria 346 (42.5%) | <i>p</i> value |
|---|---------------------------------|------------------------------|----------------|
| Age (years) | 70 (59–78) | 74 (64–82) | <0.001 |
| Gender [males/females, frequency (%)] | 322/147 (68.7/31.3) | 227/119 (65.6/34.4) | 0.365 |
| BMI [median (IR), kg/m ²] | 26.0 (24.0–28.0) | 25.8 (23.1–28.0) | 0.150 |
| Hypertension [frequency (%)] | 277 (59.1) | 247 (71.4) | <0.001 |
| Diabetes [frequency (%)] | 101 (21.5) | 99 (28.6) | 0.021 |
| EF [median (IR), %] | 50.0 (42.0–55.0) | 45.0 (35.0–55.0) | <0.001 |
| NT-pro BNP [median (IR), pg/ml] | 879 (257–2469) | 2767 (832–8302) | <0.001 |
| Tn I [median (IR), ng/ml] | 4.25 (0.21–44.85) | 7.81 (0.46–63.45) | 0.005 |
| C-Reactive protein [median (IR), mg/dl] | 9.0 (8.0–21.5) | 17.0 (9.0–57.8) | <0.001 |
| Leukocytes [median (IR), ×1000/μl] | 8.1 (6.5–10.3) | 9.7 (7.3–12.9) | <0.001 |
| Uric Acid [median (IR), mg/dl] | 5.6 (4.7–6.7) | 6.0 (5.0–7.4) | <0.001 |
| Glycemia [median (IR), g/l] | 1.08 (0.91–1.38) | 1.24 (0.98–1.69) | <0.001 |
| Fibrinogen [median (IR), mg/dl] | 426 (357–505) | 466 (400–563) | <0.001 |
| Lactate [median (IR), mmol/l] | 0.90 (0.70–1.50) | 1.50 (0.90–2.70) | <0.001 |
| eGFR [median (IR), ml/min/1.73 m ²] | 90.2 (74.8–106.8) | 72.5 (47.2–102.7) | <0.001 |
| LOS [median (IR), %] (h) | 61 (44–96) | 72 (48–120) | <0.001 |
| Dead patients [frequency (%)] | 3 (0.6%) | 30 (8.7%) | <0.001 |

BMI body mass index, *IR* interquartile range, *EF* left ventricular ejection fraction, *NT-pro BNP* N terminal pro Brain Natriuretic Peptide, *Tn I* troponin I, *eGFR* estimated Glomerular Filtration Rate, *LOS* length of stay

- Unstable angina/non-ST elevation myocardial infarction [15]
- Acute heart failure (AHF) [16]
- Dysrhythmias
- Other (i.e. stable angina, pulmonary embolism)

Table 1 depicts the clinical characteristics of the 815 patients included in the study. Men are more prevalent (67.4%), and hypertension is present in more than half of the patients (64.3%). Acute coronary syndrome (that is STEMI and UA/NSTEMI) is the most frequent admission diagnosis accounting for 71.4%. In-ICCU mortality rate was 4% (33/815).

Among patients with estimated glomerular filtration rate (eGFR) ≥ 60 ml/min/1.73 m² (who accounted for 84.4%), microalbuminuria is detectable in the 35%, while in patients with eGFR < 60 ml/min/1.73 m² it is found in 62.4%.

Table 2 depicts the comparison between the patients with microalbuminuria and those without. In our series, microalbuminuria is detectable in 39.3% (294/815 patients). Patients with microalbuminuria are older ($p < 0.001$), more hypertensive ($p < 0.001$) and diabetic (0.02). They show lower values of LVEF ($p < 0.001$) and eGFR ($p < 0.001$) and higher values of NT-pro BNP ($p < 0.001$), Tn I ($p = 0.005$), uric acid ($p < 0.001$), glycemia ($p < 0.001$) and lactate ($p < 0.001$). A higher inflammatory activation is observed in patients with microalbuminuria, as inferred by the higher values of

C-reactive protein ($p < 0.001$), leukocytes ($p < 0.001$), fibrinogen ($p < 0.001$). Length of stay is higher in patients with microalbuminuria ($p < 0.001$), as well as in-ICCU mortality rate ($p < 0.001$).

Microalbuminuria shows a significant negative correlation with LVEF (Spearman's $\rho = -0.228$; $p < 0.001$), while it is positively correlated with C-reactive protein (Spearman's $\rho = 0.239$; $p < 0.001$), NT-pro-BNP (Spearman's $\rho = 0.306$; $p < 0.001$) and glycemia (Spearman's $\rho = 0.191$; $p < 0.001$).

The following variables are independently associated with the development of microalbuminuria (when adjusted for age, hypertension, diabetes, eGFR, C-RP and EF): NT-pro BNP (100 pg/ml step: OR 1.004; 95% CI 1.002–1.007; $p = 0.002$); glycemia (1 g/dl step: OR 1.686; 95% CI 1.201 to 2.366; $p = 0.003$). Nagelkerke R^2 0.16; Hosmer–Lemeshow goodness of fit 6.329, $p = 0.610$.

At backward regression analysis, the following variables are independent predictors for in-ICCU mortality: Admission eGFR (1 ml/min/1.73m² step) (OR 0.973; 95% CI 0.959–0.988; $p < 0.001$); LVEF (1% step) (OR 0.944; 95% CI 0.914–0.975; $p < 0.001$); Microalbuminuria (1 μ g/min step) (OR 1.017; 95% CI 1.010–1.024; $p < 0.001$). Nagelkerke R^2 0.34; Hosmer–Lemeshow goodness of fit 11.626, $p = 0.169$.

Based on the ROC curve for the entire population, the optimum microalbuminuria threshold for in-ICCU death

should be 20 µg/min. This threshold would have yielded a sensitivity of 91% (95% CI 76–98%) and a specificity of 60% (95% CI 56–63%). The positive predictive value is 8.7%, while the negative predictive value is 99.4%. The corresponding RR for microalbuminuria >20 mg/dl is 13.6 (95% CI 4.5–41.7; $p < 0.001$).

Discussion

The main finding of the present investigation is that in a large cohort of consecutive acute cardiac patients, microalbuminuria on admission shows a high prevalence (being detectable in the 39.3%), and it is an independent predictor of in-ICCU mortality.

Microalbuminuria is recognized as a strong and independent indicator of increased cardiovascular risk among subjects with and without diabetes [17], its presence substantially increases the cardiovascular risk, and it is an independent predictor of ischemic heart disease in a population-based cohort [18]. In chronic heart failure, elevated albumin excretion is a powerful prognostic marker for all-cause mortality, independent of diabetes, hypertension, or renal function [19].

Our series includes mainly patients with acute coronary syndromes who undergo mechanical revascularization (accounting for 71.4% of the entire population), but available evidence of the prognostic significance of microalbuminuria in these patients is so far controversial. In patients with acute myocardial infarction (AMI) [20–22] microalbuminuria has been reported to occur early, yielding prognostic information about in-hospital mortality additional to that provided by clinical or echocardiographic evaluation of left ventricular function. In non-diabetic patients with AMI [23], microalbuminuria has been shown to be a predictor not only for mortality but even for morbidity. In hypertensive patients with AMI [24], the combination between microalbuminuria and hypertension is associated with a higher risk of in-hospital mortality, independent of other possible confounders (such as heart failure). Previous investigations have been performed in heterogeneous populations of patients with hypertension and myocardial infarction, diabetic and non-diabetic, submitted either to thrombolysis or to mechanical revascularization or not revascularized. Conversely, in our paper [25], in the early phase of 257 STEMI hypertensive patients without previously known diabetes all submitted to mechanical revascularization, microalbuminuria, though a common finding, did not yield prognostic information about in-hospital mortality or complications.

In the present investigation, microalbuminuria shows a strong independent prognostic role for early mortality, independent of the admission diagnosis. This can be

probably related to the fact that microalbuminuria is strictly linked to the inflammatory activation (as inferred by C-RP) and glucose values, as a part of the acute stress response. C-RP is a well known prognostic marker in cardiovascular diseases, both in chronic and acute cardiac conditions [26–29]. In a previous paper [25] performed in hypertensive non-diabetic STEMI patients, microalbuminuria was associated with acute glucose dysmetabolism (as inferred by hyperglycemia and the prevalence of insulin-resistance), thus suggesting that it can be considered as the part of the acute metabolic response to stress.

In our series, microalbuminuria correlates with NT-pro BNP values, which is known as a strong predictor for cardiovascular mortality [30]. Our findings are in agreement with recent investigations performed in humans [31] and in animal models [32]. In Japanese hypertensive patients, a concomitant reduction in BNP and microalbuminuria is observed after therapy [33], while in hypertensive rats, microalbuminuria is significantly correlated with reductions in cardiac mass and hypertrophy markers (such as BNP), thus suggesting a potential link between microalbuminuria and BNP. In the acute phase of STEMI [10], NT-pro BNP is related to the extension of myocardial injury (as inferred by peak Tn I), and to inflammatory activation (as indicated by C-RP). It is an independent predictor for early mortality.

The main limitation of the present study is that it comprises unselected patients admitted to our ICCU because of varying diagnoses (from acute coronary syndrome to acute pulmonary embolism). On the other hand, our population including consecutive acute cardiac patients, reflects the “contemporary clinical practice” in an ICCU of a tertiary center.

In conclusion, in the acute phase of cardiac patients, microalbuminuria is a common finding and it represents an independent predictor for early mortality. It is strictly linked to the inflammatory activation (as indicated by C-RP) and to acute glucose values, thus suggesting that it is the part of the acute response to stress.

Conflict of interest None.

References

1. Pedersen LM (1999) Clinical significance of urinary albumin excretion in patients with non-Hodgkin's lymphoma. *Br J Haematol* 107:889–891
2. Pedersen LM, Milman N (1998) Microalbuminuria in patients with lung cancer. *Eur J Cancer* 34:76–80
3. Smith CT, Gosling P, Sanghera K et al (1994) Microproteinuria predicts the severity of systemic effects of reperfusion injury following infra renal aortic aneurysm surgery. *Ann Vasc Surg* 8:1–5
4. Shearman CP, Gosling P (1989) Walker KJ: Is low proteinuria an early predictor of severity of acute pancreatitis? *J Clin Path* 42:1132–1135

5. De Gaudio AR, Spina R (1999) Glomerular permeability and trauma: a correlation between microalbuminuria and injury severity score. *Crit Care Med* 27:2105–2108
6. Gopal S, Carr B, Nelson P (2006) Does microalbuminuria predict illness severity in critically ill patients on the intensive care unit? A systematic review. *Crit Care Med* 34(6):1805–1810
7. Abid O, Sun Q, Sugimoto K, Mercan D, Vincent JL (2001) Predictive value of microalbuminuria in medical ICU patients: results of a pilot study. *Chest* 120(6):1984–1988
8. Gosling P, Czyz J, Nightingale P, Manji M (2006) Microalbuminuria in the intensive care unit: Clinical correlates and association with outcomes in 431 patients. *Crit Care Med* 34(8):2158–2166
9. Thorevska N, Sabahi R, Upadya A, Manthous C, Amoateng-Adjepong Y (2003) Microalbuminuria in critically ill medical patients: prevalence, predictors, and prognostic significance. *Crit Care Med* 31(4):1075–1081
10. Donnelly R, Yeung JM, Manning G (2003) Microalbuminuria: a common, independent cardiovascular risk factor, especially but not exclusively in type 2 diabetes. *J Hypertens Suppl* 21:S7–S12
11. Lazzeri C, Valente S, Chiostrì M, Sori A, Bernardo P, Gensini GF (2010) Uric acid in the acute phase of ST elevation myocardial infarction submitted to primary PCI: its prognostic role and relation with inflammatory markers: a single center experience. *Int J Cardiol* 138(2):206–209
12. Valente S, Lazzeri C, Chiostrì M, Giglioli C, Sori A et al (2009) NT-proBNP on admission for early risk stratification in STEMI patients submitted to PCI. Relation with extension of STEMI and inflammatory markers. *Int J Cardiol* 132(1):84–89
13. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, Kusek JW, Eggers P, Van Lente F, Greene T, Coresh J, CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) (2009) A new equation to estimate glomerular filtration rate. *Ann Intern Med* 150(9):604–612
14. European Association for Percutaneous Cardiovascular Interventions, Wijns W, Kolh P, Danchin N, Di Mario C, Falk V, Folliquet T, Garg S, Huber K, James S, Knuuti J, Lopez-Sendon J, Marco J, Menicanti L, Ostojic M, Piepoli MF, Pirllet C, Pomar JL, Reifart N, Ribichini FL, Schali J, Sergeant P, Serruys PW, Silber S, Sousa Uva M, Taggart D; ESC Committee for Practice Guidelines, Vahanian A, Auricchio A, Bax J, Ceconi C, Dean V, Filippatos G, Funck-Brentano C, Hobbs R, Kearney P, McDonagh T, Popescu BA, Reiner Z, Sechtem U, Sirnes PA, Tendera M, Vardas PE, Widimsky P; EACTS Clinical Guidelines Committee, Kolh P, Alfieri O, Dunning J, Elia S, Kappetein P, Lockowandt U, Sarris G, Vouhe P, Kearney P, von Segesser L, Agewall S, Aladashvili A, Alexopoulos D, Antunes MJ, Atalar E, Brutel de la Riviere A, Doganov A, Eha J, Fajadet J, Ferreira R, Garot J, Halcox J, Hasin Y, Janssens S, Kervinen K, Laufer G, Legrand V, Nashef SA, Neumann FJ, Niemela K, Nihoyannopoulos P, Noc M, Piek JJ, Pirk J, Rozenman Y, Sabate M, Starc R, Thielmann M, Wheatley DJ, Windecker S, Zembala M (2010) Guidelines on myocardial revascularization: the task force on myocardial revascularization of the european society of cardiology (esc) and the european association for cardio-thoracic surgery (EACTS). *Eur Heart J* 31(20):2501–55
15. ACC/AHA Guidelines for the management of patients with unstable angina/non ST-elevation myocardial infarction guidelines *Medicine Circulation* (2007) 116: e148–e304
16. Sharon AH, William TA, Marshall HC et al (2009) Focused update incorporated into the acc/aha 2005 guidelines for the diagnosis and management of heart failure in adults. *J Am Coll Cardiol* 53:e1–e90
17. Stehouwer CD, Smulders YM (2006) Microalbuminuria and risk for cardiovascular disease: analysis of potential mechanisms. *J Am Soc Nephrol* 17(8):2106–2111
18. Borch-Johnsen K, Feldt-Rasmussen B, Strandgaard S (1999) Urinary albumin excretion: an independent predictor of ischemic heart disease. *Arterioscler Thromb Vasc Biol* 19:1992–1997
19. Masson S, Latini R, Milani V, Moretti L, Rossi MG, Carbonieri E, Frisinghelli A, Minneci C, Valisi M, Maggioni AP, Marchioli R, Tognoni G, Tavazzi L, GISSI-HF Investigators (2010) Prevalence and prognostic value of elevated urinary albumin excretion in patients with chronic heart failure: data from the GISSI-Heart Failure trial. *Circ Heart Fail* 3(1):65–72
20. Taskiran M, Feldt-Rasmussen B, Jensen GB, Jensen JS (1998) Urinary albumin excretion in hospitalized patients with acute myocardial infarction. Prevalence of microalbuminuria and correlation to left ventricle wall thickness. *Scand Cardiovasc J* 32(3):163–166
21. Gosling P, Hughes EA, Reynolds TM, Fox JP (1991) Microalbuminuria is an early response following acute myocardial infarction. *Eur Heart J* 12(4):508–513
22. Berton G, Citro T, Palmieri R, Petucco S, De Toni R, Palatini P (1997) Albumin excretion rate increases during acute myocardial infarction and strongly predicts early mortality. *Circulation* 96(10):3338–3345
23. Lekatsas I, Koulouris S, Triantafyllou K, Chrisanthopoulou G, Moutsatsou-Ladikou P, Ioannidis G et al (2006) Prognostic significance of microalbuminuria in non-diabetic patients with acute myocardial infarction. *Int J Cardiol* 106(2):218–223
24. Berton G, Cordiano R, Mbaso S, De Toni R, Mormino P, Palatini P (1998) Prognostic significance of hypertension and albuminuria for early mortality after acute myocardial infarction. *J Hypertens* 16(4):525–530
25. Lazzeri C, Valente S, Chiostrì M, Picariello C, Gensini GF (2010) Microalbuminuria in hypertensive nondiabetic patients with ST elevation myocardial infarction. *J Cardiovasc Med (Hagerstown)* 11(10):748–753
26. The MONICA/KORA Myocardial Infarction Registry, Meisinger C, Heier M, von Scheidt W, Kuch B (2010) Admission C-reactive protein and short- as well as long-term mortality in diabetic versus non-diabetic patients with incident myocardial infarction. *Clin Res Cardiol* 99(12):817–823
27. Araújo JP, Lourenço P, Azevedo A, Friões F, Rocha-Gonçalves F, Ferreira A, Bettencourt P (2009) Prognostic value of high-sensitivity C-reactive protein in heart failure: a systematic review. *J Card Fail* 15(3):256–266
28. He LP, Tang XY, Ling WH, Chen WQ, Chen YM (2010) Early C-reactive protein in the prediction of long-term outcomes after acute coronary syndromes: a meta-analysis of longitudinal studies. *Heart* 96(5):339–346
29. Genest J (2010) C-reactive protein: risk factor, biomarker and/or therapeutic target? *Can J Cardiol* 26(Suppl A):41A–44A
30. Struthers A, Lang C (2007) The potential to improve primary prevention in the future by using BNP/N-BNP as an indicator of silent ‘pancardiac’ target organ damage: BNP/N-BNP could become for the heart what microalbuminuria is for the kidney. *Eur Heart J* 28(14):1678–1682
31. Uno H, Ishikawa J, Hoshida S, Kabutoya T, Ishikawa S, Shimada K, Kario K (2008) Effects of strict blood pressure control by a long-acting calcium channel blocker on brain natriuretic peptide and urinary albumin excretion rate in Japanese hypertensive patients. *Hypertens Res* 31(5):887–896
32. Saliba Y, Chouery E, Mégarbané A, Jabbour H, Fares N (2010) Microalbuminuria versus brain natriuretic peptide in cardiac hypertrophy of hypertensive rats. *Physiol Res* 59(6):871–880